We claim:

1. A method of generating a cell comprising a stably replicating sub-genomic viral replicon, said method comprising

a) disabling a host anti-viral response factor in said cell, and

b) introducing said sub-genomic viral replicon into said cell.

2. A method according to claim 1, wherein said host anti-viral response factor is PKR activity.

3. The method of claim 2 wherein PKR activity in said cell is disabled by expressing a dominant-negative PKR, mutating at least one copy of the endogenous PKR gene, adding 5-amino purine, expressing $p58^{IPK}$ protein, expressing hepatitis C virus (HCV) E2, and using a PKR antisense nucleic acid.

4. The method of claim 3 wherein PKR activity in said cell is disabled by expressing a dominant-negative PKR.

5. The method of claim 3 wherein PKR activity in said cell is disabled by expressing $p58^{IPK}$ protein.

6. The method of claim 3 wherein PKR activity in said cell is disabled by mutating at least one copy of the endogenous PKR gene.

7. The method of claim 3 wherein PKR activity in said cell is disabled by adding 5-amino purine.

8. The method of claim 3 wherein PKR activity in said cell is disabled by expressing HCV E2.

9. The method of claim 3 wherein PKR activity in said cell is disabled by using PKR

antisense nucleic acid.

10. The method of claim 1 wherein the sub-genomic viral replicon is an HCV sub-genomic replicon, a Sindbis virus sub-genomic replicon, a poliovirus sub-genomic replicon, or a bovine viral diarrhea virus (BVDV) sub-genomic replicon.

11. The method of claim 10 wherein the sub-genomic viral replicon is an HCV sub-genomic replicon.

12. The method of claim 10 wherein the sub-genomic viral replicon is a Sindbis virus sub-genomic replicon.

13. The method of claim 10 wherein the sub-genomic viral replicon is a poliovirus sub-genomic replicon.

14. The method of claim 10 wherein the sub-genomic viral replicon is a BVDV sub-genomic replicon.

15. The method of claim 2 wherein the sub-genomic viral replicon is an HCV sub-genomic replicon, a Sindbis virus sub-genomic replicon, a poliovirus sub-genomic replicon, or a bovine viral diarrhea virus (BVDV) sub-genomic replicon.

16. The method of claim 15 wherein the sub-genomic viral replicon is an HCV sub-genomic replicon.

17. The method of claim 15 wherein the sub-genomic viral replicon is a Sindbis virus sub-genomic replicon.

18. The method of claim 15 wherein the sub-genomic viral replicon is a poliovirus sub-genomic replicon.

19. The method of claim 15 wherein the sub-genomic viral replicon is a BVDV sub-genomic replicon.

20. The method of claim 15 wherein PKR activity in said cell is disabled by expressing a dominant-negative PKR, mutating at least one copy of the endogenous PKR gene, adding 5-amino purine, expressing $p58^{IPK}$, expressing HCV E2, or using PKR antisense nucleic acid.

21. The method of claim 20 wherein PKR activity in said cell is disabled by expressing a dominant-negative PKR.

22. The method of claim 20 wherein PKR activity in said cell is disabled by mutating at least one copy of the endogenous PKR gene.

23. The method of claim 20 wherein PKR activity in said cell is disabled by adding 5-amino purine.

24. The method of claim 20 wherein PKR activity in said cell is disabled by expressing $p58^{IPK}$.

25. The method of claim 20 wherein PKR activity in said cell is disabled by expressing HCV E2.

26. The method of claim 20 wherein PKR activity in said cell is disabled by using PKR antisense nucleic acid.

27. A method of generating a cell comprising a stably replicating sub-genomic viral replicon, said method comprising introducing said sub-genomic viral replicon into a cell wherein PKR activity has been disabled.

28. A cell produced by the method of any of claims 1, 2 or 27.

29. A cell comprising a replicating sub-genomic viral replicon wherein said cell is PKR deficient.

30. The cell of claim 29 wherein the sub-genomic viral replicon is a HCV sub-genomic replicon.

31. The cell of claim 30 wherein the HCV sub-genomic replicon comprises all of the non-structural HCV genes and none of the structural HCV genes.

32. A method of screening for compounds that modulate viral replication comprising the steps of

a) administering a test compound to a cell according to claim 28, and

b) determining whether said test compound modulates the replication of said sub-genomic viral replicon.

33. A method of screening for compounds that modulate viral replication comprising the steps of

a) administering a test compound to a cell according to claim 29, and

b) determining whether said test compound modulates the replication of said sub-genomic viral replicon.

34. A method of screening for compounds that modulate HCV replication comprising the steps of

a) administering a test compound to a cell according to claim 30, and

b) determining whether said test compound modulates the replication of said HCV sub-genomic replicon.

35. A method of screening for compounds that modulate HCV replication comprising the steps of

a) administering a test compound to a cell according to claim 31, and

b) determining whether said test compound modulates the replication of said HCV sub-genomic replicon.

36. A method of screening for compounds that inhibit viral replication comprising

a) administering a test compound to a cell according to claim 28, and

b) determining whether the test compound inhibits the replication of said sub-genomic viral replicon.

37. A method of screening for compounds that inhibit viral replication comprising the steps of

a) administering a test compound to a cell according to claim 29, and

b) determining whether said test compound inhibits the replication of said sub-genomic viral replicon.

38. A method of screening for compounds that inhibit HCV replication comprising the steps of

a) administering a test compound to a cell according to claim 30, and

b) determining whether said test compound inhibits the replication of said HCV sub-genomic replicon.

39. A method of screening for compounds that inhibit HCV replication comprising the steps of

a) administering a test compound to a cell according to claim 31, and

b) determining whether said test compound inhibits the replication of said HCV sub-genomic replicon.